JAPANESE MEDICAL MATERIAL

RODEALIN

(Preparations of Rhodea Japonica Roth)

Report No. 248

24 July 1946

MEDICAL ANALYSIS SECTION
5250th Technical Intelligence Company
APO 500

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SOURCE: Tokyo, Japan.

IMPORTANCE: Not previously reported. A glucosidal preparation of Rhodea japonica Roth claimed to be a cardiac stimulant and diuretic. No identical product is listed in available standard American references.

DESCRIPTION: Ten glass ampuls, each containing 1.0 cc. of a clear colorless solution are packaged in a cardboard box.

Twenty-five grams of a fine white powder are contained in a cardboard carton.

SUMMARY OF GENERAL INFORMATION: Rodealin contains the glucoside, Rhodein, extracted from Rhodea japonica Roth, a plant indigenous to Japan. The glucoside is claimed to possess cardiac stimulant and diuretic properties. The product is available in the form of an injection, a solution for oral use, a diluted powder, and as tablets. The literature claims that it is a more effective cardiac stimulant and diuretic than digitalis and that its cumulative action is intermediate between that of digitalis and strophanthin.

A summary of pertinent information is recorded in TOYOKICHI TAKASE's book, "Chemical Structure and Physiological Action", Volume II, page 1413, from which the following is extracted:

"Rodealin is a product containing the active ingredients of Rhodea japonica Roth.

"Rodealin contains Rhodein, a heart stimulating glucoside. It has a powerful diuretic and heart stimulating action and its lethal dose in cats is 1 cc. of the injection, 1 cc. of the solution, or 0.5 gm. of the powder (0.1 gm. of powder diluted 5 times) per kilogram of body weight.

"This product has an intermediate action between that of Digitoxin and Strophanthin. Therefore, compared to Digitalis products, this can be applied with more safety in acute and chronic cases. When 3 - 4 cc. per day is administered it reduces the pulse and increases the urine after 2 - 5 days. The adult dose is 4 - 6 cc. per day, powder 0.4 - 0.6 gm. per day, and injection 1.0 - 2.0 cc. per day."*

* Taiichi Murashima - Tohoku Journ. exp. Med. 8, 405 (1927)
Keisuke Yamanouchi - Tohoku Journ. exp. Med. 9,111 (1927)
Minoru Hatano & Keishiro Saijo - Tohoku Journ. exp. Med. 565 (1936)
Seichi Yagi - Treatment and Prescription, 9,111 (1928)
Shuzo Ozawa, Shigeji Tsuyi, Eeikei Koide, Hachero Takata - Summary of Treatment 1, 1 (1932)
Takeshi Itakura - Magazine on Treatment, 3, 576 (1933)"

The literature enclosed with the product has been translated, embodied in this report, and includes its action, indications, directions and dosage, therapy, remarks, packaging and manufacturer. No results of comparative tests against other well-known cardiac Stimulants are presented.

No reference is made in available American texbooks to either the plant, Rhodea japonica Roth, or its glucoside, Rhodein.

PHOTOGRAPHS:

Figure 1 - Closed packages of Rodealin, Ampoules and Powder

Figure 2 - Open packages of Rodealin, Ampoules and Powder

Figure 3 - Rodealin literature

Figure 4 - Additional Rodealin literature

Figure 1 - Closed Packages of Rodealin Ampoules and Powder.

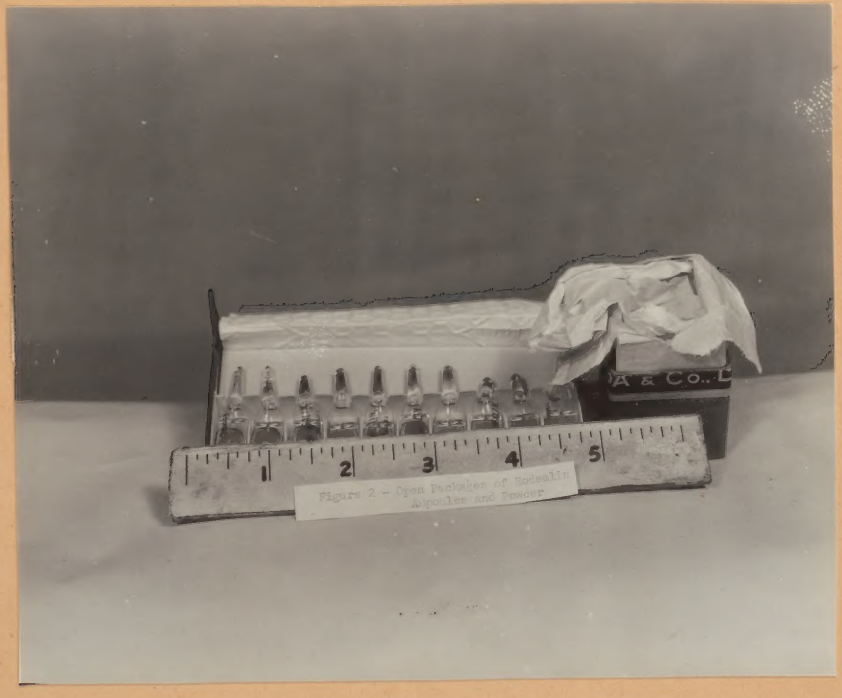

Figure 2 - Open Packages of Rodealin Ampoules and Powder

ロデアリン

【本　質】

ロデアリンは東北帝國大學敎授醫學博士八木精一氏（醫學部藥物學敎室）指導のもとに醫學博士村島泰一氏、醫學博士山内惠助氏、醫學博士高瀨豊吉氏等によつて行はれたる日本産植物萬年青 Rhodea japonica Roth 成分の强心・利尿作用に關する藥物學的研究に基ける製品なり。

一、注射液（皮下、筋肉内、靜脈内注射用）はヘツチヤー、ブロデイー氏法致死量、體重毎廷約一・〇ccの力價を有し特に注射局所に刺戟疼痛を來すべき成分の除去操作を施せり。從つて鎭痛藥を含有せず。

二、内服用液一・〇ccは注射液一・〇ccに對應し、アルコール一〇%、グリセリン五%を含有す。

三、内服用粉末〇・一瓦は、注射液一・〇ccに對應す。

四、内服用錠劑一錠は内服用粉末〇・一瓦を含有し、注射液一・〇cc、内服用液一・〇ccに對應す。

【效　能】

一、心臟の收縮及び擴張を强大ならしめ搏出量の增加を來し不整搏動を調整し且つ心臟絶對力の著明なる增加を來す。その作用はヂギタリス葉の成分よりも强し。

二、腎血管を擴大し腎血流を增加せしめ著明なる尿量增加を來し、冠狀血管を擴大して心臟の榮養を佳良ならしめ且つ腸血管を縮小して腹部に鬱積せる多量の血液を心臟に供給し以て心作業量の增加に資す。その作用はヂギタリス葉の成分よりも强し。

三、迷走神經中樞を興奮して心臟搏動の緩徐を來すが故に、心臟衰弱狀態に於ては前述作用と相俟つて良好なる效果を齎す。その作用はヂギタリス葉の成分よりも强し。

四、蓄積能はヂギトキシンとストロファンチンとの中間に位す。即ちヂギタリス製劑よりも安全に急性・慢性疾患とも共に應用し得べし。

五、局所刺戟作用、催吐作用はヂギタリス葉の成分よりも弱し。

◇腸チフス、肺炎、肺結核その他諸疾患に於ける心機能不全の治療及び豫防。

◇腎臟疾患、肋膜炎、腹膜炎、肝臟疾患、心機能不全等に於ける浮腫、腹水、水分滯溜の治療。

◇心房震顫及び其の他の不整脈の治療。

【用法及用量】

注　射

一、一般に一回一・〇―二・〇ccを皮下又は筋肉内に注射し必要に應じて反復す。二・〇cc以上多量を用ふる場合には筋肉内注射を選び、注射後は局所をよく按摩するを可とす。急速を要せざる場合には、一・〇cc宛を數時間毎に注射し、又は二・〇cc宛を朝夕に注射す。

二、稍强き作用を要すべき場合には一回二・〇cc宛、三時間毎に注射すれば、數回の注射後に强心利尿作用發現す。急を要する場合には靜脈内に注射す。一般に一・〇―四・〇ccを徐々に注射す。ロヂノン（一〇―五〇%）五・〇―一〇・〇ccを混合するを可とす。

三、急速に强力・確實なる作用を要すべき場合には比較的大量を短時間内に用ふ。

△此の場合、原則として體重五〇瓩に對して第一回に五・〇ccを筋肉内注射し、次に第二回を三時間後に三・〇cc、更に第三回を三時間後に二・〇cc、第四回以後は三時間毎に一・〇cc宛を用ふ。勿論此の際毎回注射前にロデアリンの作用の有無を觀察し、その作用を明かに認むる時は適用を中止し、以後數時間毎に患者を觀察し、必要に應じて注射を行ふ。

△極めて救急の場合、數時間内に强力作用を要すべき場合には、體重五〇瓩に對する必要量一〇・〇ccを一回に筋肉内に注射す。斯くして心搏數減少、脈搏脫落の消失、尿量の著明なる增加、體重減少等の作用が速きは二〇分、通例二時間前後に現はる。若し一回の必要量注射にて十分なる作用現はれざる時は、三時間後に一・〇ccを注射し、必要に應じて三時間毎に一・〇cc注射を反復す。

内　服

液　劑　△一般に成人一日量三・〇―四・〇ccを用ふ。一般に服用二―五日にして脈搏減少、尿量增加を認む。

△小用量（小人用量の謂に非ず）としては一日量一・五―三・〇ccを用ふ。

△大用量としては一日量四・〇―六・〇ccを用ふ。

必要に應じて一日量八・〇ccに及ぶ。

粉　末　△一般に一日量〇・三―〇・四瓦を用ふ。

△小用量（小人用量の謂に非ず）としては一日量〇・一五―〇・三瓦を用ふ。

△大用量としては一日量〇・四―〇・六瓦を用ふ。

必要に應じて一日量〇・八瓦に及ぶ。

五倍用粉末　（本品一瓦は前記粉末の〇・二瓦又は液劑の二ccに當る）即ち一般に一日量一・五―二・〇瓦を用ふ。

△小用量としては一日量〇・七五―一・五瓦を用ふ。

△大用量としては一日量二・〇―三・〇瓦を用ふ。

必要に應じて一日量四・〇瓦に及ぶ。

錠　劑　△通常一日量三―四錠を用ふ。

△小用量（小人用量の謂に非ず）としては一日量一錠半―三錠を用ふ。

△大用量としては一日量四―六錠を用ふ。

必要に應じて一日量八錠に及ぶ。

△浮腫、體液滯溜の甚しき場合には、ロデアリン液一日量四・〇cc以上と醋酸カリ液（五・〇―一〇・〇cc）との併用によつて强力著明なる尿量增加を期待し得べし。

△内服には空胃時を選び、靜脈内注射にはカルシウム塩、ロヂノン又はロヂノン・カルシウムを併用せば其效特に著し。

【維持療法に就て】

體内に吸收せられたるロデアリンは、時の經過と共に體内より消失す。仍て治療後に心機能不全を再發するが如き場合には、はじめの治療作用を維持せんがために消失量に匹敵すべきロデアリンを追加使用せざるべからず。

即ち確實なるロデアリンの作用發現の翌日より一般に體重一瓩に對し一日平均〇・〇三cc宛を、例へば體重五〇瓩に對し平均一日一・六cc宛を用ひ、狀態に應じて增減す。

（注　意）内服用液劑及び粉末を溶解せるものは注射用に適せず。粉末並びに五倍用末は今般資材關係により從來の可溶性賦形劑を廢し、不溶性賦形劑を使用せるを以て水劑としての處方は避けられたし。粉末は濾檢して貯ふべし。

【包　裝】

注射液　一〇管　五〇管
（一・〇cc）　（二・〇cc）
一〇〇cc　一〇〇cc

内服用液　一〇瓦　二五瓦
クロ粉末　五〇瓦　一〇〇瓦
（五倍用）　一〇〇瓦　二五〇瓦
クロ錠劑　（〇・一）三錠　二五錠

製造發賣元　武田藥品工業株式會社
大阪市東區道修町二丁目二七

第　信　**Figure 4 - Additional Rodealin Literature**

報告用箋

Rodealin

ロデアリン注射液

蘭草青ヲ細剉乾燥シ石油エーテルニテ樹脂様物質ヲ除キ水浸濾別シ母液ヲ減圧下ニ濃縮シテエキス状トナシアルコールニ浸出シ不溶分ヲ除去シエーテルヲ加ヘ有毒性物質ヲ沈澱セシメ濾過除去シタル後アルコール、エーテルヲ蒸溜シ放冷スレバ有効物質ハ結晶性粉末トシテ析出ス。コノ結晶性粉末ヲ集メアルコールニテ再結晶精製ス　本結晶ヲ百万倍食塩0.三%塩化カルシウム0.二%含有蒸溜水ニ溶解シ「パッサーブロッチー」法ニ據リテ力價ヲ検定シアンプル中ニ熔閉シ製ス、

武田薬品工業株式會社

TRANSLATION OF ACCOMPANYING LITERATURE

RODEALIN

GENERAL:

Rodealin is a preparation which was manufactured after extensive medicinal study with regards to the stimulating and diuretic action of the Japanese plant "Rhodea Japonica Roth". Three Japanese doctors were instrumental in the studies of this plant. They are Hataichi Murayama, Keisuke Yamanouchi, and Toyokichi Takase. All three worked under the supervision of Dr. Seiichi Yagi, a professor at the Tohoku Imperial University.

1. Rodealin injections (subcutaneous, intravenous, intramuscular), can produce an effect equivalent to a lethal dose by Hatcher and Brodie's method, namely about 1.0 cc. per kilogram of body weight. Rodealin does not irritate or cause any pain at the point of injection even though it contains no anodyne.
2. 1.0 cc. of liquid Rodealin for oral use is equivalent to 1.0 cc. of the injection and contains 10% alcohol and 5% glycerin.
3. 0.1 gram of powdered Rodealin for oral use is equivalent to 1.0 cc. of the injectionable liquid.
4. One Rodealin tablet for oral use contains 0.1 gram of powder and is equivalent to 1.0 cc. of the liquid for oral use.

INDICATIONS:

1. Rodealin tends to strengthen heart contraction and expansion, increases heart flow, corrects irregular pulsation, and stimulates the heart to its maximum efficiency. The active ingredient in Rodealin is more effective than digitalis in the treatment of heart disorders.
2. Rodealin expands the blood vessels of the kidney thereby increasing the blood in the kidney and causing a marked increase of urine and it expands the coronary blood vessels and strengthens the heart. It reduces the size of the intestinal blood vessels and sends a large quantity of the blood which is collected in the abdominal region into the heart, strengthening heart action. This action is stronger than that of Digitalis leaves.
3. Rodealin stimulates the vagus, thus slowing heart pulsation and resulting in a correction of debility of the heart. This action is stronger than that of Digitalis leaves.
4. The cumulative action is intermediate between digitalis and strophanthin. In acute and chronic ailments, it may be employed with greater safety than digitalis.
5. The irritating and emetic actions of Rodealin are more moderate than those of digitalis in the prophylaxis and treatment of heart disorders caused by typhoid, pneumonia, and tuberculosis, in the treatment of dropsy and ascites caused by

Kidney diseases, pleurisy, peritonitis, liver diseases, heart disorders, and in the treatment of heart murmurs and abnormal or irregular pulse.

DIRECTIONS AND DOSAGE:

1. Subcutaneous or intramuscular, 1.0 - 2.0 cc. injections repeated as necessary. Following each intramuscular injection, the area should be well massaged. In common ailments inject 1.0 cc. every few hours or 2.0 cc. morning and evening.
2. When larger doses are necessary, or intensive medication is desired, inject 2.0 cc. every three hours. This dosage will produce a heart stimulating and diuretic action. For intravenous medication, 1.0 to 4.0 cc., mixed with 5.0 to 10.0 cc. of glucose solution (10 - 50%) may be employed.
3. For rapid medication, a large quantity of Rodealin may be injected within a short period of time. As a rule, for each 50 kg. of body weight, the following quantities may be employed:

    1st injection - 5.0 cc. - Intramuscularly
    2nd injection - 3.0 cc. - Intramuscularly after 3 hours
    3rd injection - 2.0 cc. - Intramuscularly after 3 hours
    Subsequent injections- 1.0 cc. - Intramuscularly every 3 hours

Observation of the patient must be made prior to each injection. One dose of 10.0 cc. of Rodealin intramuscularly may be used to obtain a strong reaction within several hours. Effective therapeutic results will appear within 20 minutes at the earliest but usually after about two hours. Repeated injections of 1.0 cc. every three hours may be used if necessary.

ORAL ADMINISTRATION:

Adults:

Liquid Rodealin:

General dose - 3.0 - 4.0 cc. daily.
Reduction of pulsation and increase of urinary output in 2 - 5 days.
Small dose: 1.5 - 3.0 cc. daily.
Large dose: 4.0 - 6.0 cc. daily. (8.0 cc. maximum).

Powdered Rodealin:

General dose: 0.3 - 0.4 gm. daily.
Small dose: 0.15 - 0.3 gm. daily.
Large dose: 0.4 - 0.6 gm. daily. (0.8 gm. maximum).

Powdered Rodealin - dilute: 20% (1 gm. is equivalent to 0.2 gm. of Rodealin powder or 2.0 cc. Liquid Rodealin).

General dose: 1.5 - 2.0 gm. daily.
Small dose: 0.75 - 1.5 gm. daily.
Large dose: 2.0 - 3.0 gm. daily. (4.0 gm. maximum).

Tablets Rodealin:

General dose: 3 - 4 tablets daily.
Small dose: 1½ 3 tablets daily.
Large dose: 4 - 6 tablets daily. (8 tablets maximum).

In the treatment of dropsy, a marked increase of urine results from the use of 4.0 cc. of Rodealin solution with 5.0 to 10.0 cc. of Potassium acetate solution. Oral administration of Rodealin should be made at the time when the stomach is empty. The effectiveness of injected Rodealin is increased by the use of a calcium salt with glucose.

PROCEDURE FOR THERAPEUTIC CONTINUITY:

Rodealin, which has been absorbed, disappers from the body in time. Therefore, in case the heart function still seem imperfect after treatment, administer additional Rodealin equivalent to the initial dosage in order to maintain its therapeutic action.

The day following the initial appearance of Rodealin's action, administer an average dose of 0.032 cc. per 1 kg. of body weight daily, e.g. an average dose of 1.6 cc. daily per 50 Kg. of body weight. However, the quantity administered should be increased or decreased in accordance with existing conditions.

REMARKS:

Rodealin liquid or the powder in solution are not applicable as an injection. Rodealin powder is prepared by diluting Rodealin extract with an insoluble powdered diluent, therefore the powder cannot be dissolved in a liquid for use as an injection. The powder should be preserved in tightly sealed containers.

PACKAGING:

Ampuls (1.0 cc.) 10 amp. 50 amp.
Ampuls (2.0 cc.) 10 amp. 50 amp.

Liquid 100 cc. 500 cc.

Powder 10 gm. 25 gm. 100 gm. 250 gm.
Powder (Diluted) 25 gm. 250 gm. 500 gm.

Tablets (0.1) 12 tab. 25 tab. 60 tab. 150 tab.

PREPARED AND DISTRIBUTED BY:

Takeda Drug Industrial Co., Ltd.
No. 27, 2-Chome, Doshu-cho, Higashi-Ku, Osaka.